REMARKS

I. AMENDMENTS TO THE CLAIMS AND SPECIFICATION

Applicants have amended claims 22, 26, 28, 29, 34, 36, 38, 40, 41 and 46 and have canceled claims 30-33 and 42-45 to expedite prosecution. Support for the claim amendments can be found throughout the specification and originally filed claims. Accordingly, the claim amendments do not introduce new matter to the presently pending application.

In response to the objections to the specification, Applicants have amended the specification to include a section header demarcating the drawings section. Applicants note that the brief section of the drawings was previously highlighted in their April 21, 2006 response to office action. The amendments to the specification do not introduce new matter to the presently pending application.

II. THE OFFICE ACTION OF JULY 6, 2006

A. The Written Description Rejection of Claims 22-47 is Traversed

The Final Office Action of July 6, 2006 rejected claims 22-47 under 35 U.S.C. 112, first paragraph, as allegedly "failing to comply with the written description requirement." *Final Office Action of July 6, 2006*, page 2. Specifically, the Office Action alleges that the "claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *Final Office Action of July 6, 2006*, page 2. Furthermore, the Final Office Action states that the specification "has not disclosed any examples of recombinant MHC-type or recombinant HLA type molecules..." *Final Office Action of July 6, 2006*, page 4.

Applicants respectfully disagree with the Office Action and assert that the specification fully supports the claimed invention. In particular, the presently claimed invention is drawn towards methods of depleting anti-MHC antibodies in a sample using recombinant MHC molecules or recombinant MHC-type molecules, but is not directed to the recombinant MHC

molecules themselves. In other words, the present claims do not claim recombinant MHC molecules *per se*, but instead they claim methods of using these recombinant MHC molecules and recombinant MHC type molecules to deplete anti-MHC antibodies.

While recombinant MHC molecules, or variants thereof, are elements of the claims, and therefore necessary for performance of the methods, there is no requirement that the specification disclose nucleic acid sequences encoding such recombinant MHC molecules or variants thereof. To the contrary, the present claims and specification state that the recombinant MHC molecules must have a known identity and that the detected antibodies be specific for naturally occurring MHC alleles. Indeed, the specification states that "[t]hese recombinant MAC or MHC-type monomers, functioning as anti-MHC antibody antigens, have the advantage that the identity of the MHC is known." United States Pregrant Publication No. 2003/0017447 A1, ¶0017 (emphasis added). Furthermore, the specification indicates that, to detect anti-MHC antibodies, the recombinant MHC molecules should maintain "not only residues at the epitopic site, but also key skeletal residues to achieve correct folding of the MHC molecule to form the epitopic site." United States Pregrant Publication No. 2003/0017447 A1, ¶0026. Thus, the specification indicates that, contrary to the Examiner's interpretation of the claims, the recombinant MHC molecules or MHC type molecules should be produced to preserve epitopic sites, which were well known in the art at the time of filing.

Particularly relevant to the presently claimed invention, the Federal Circuit, in overturning a decision by the Board of Patent Appeals and Interferences ("the Board"), recently clarified the written description requirement in the context of claims that utilize known biological materials in *Capon et al. v. Eshhar et al. v. Dudas,* 418 F.3d 1349 (Fed. Cir., 2005). Specifically, *Capon* clarifies the written description requirement as delineated by *Eli Lilly* and *Enzo,* among others.

In *Capon*, the claims involved in the interference were directed to a chimeric gene, which "combines segments of DNA in a way that does not occur in nature." *Capon* at 1351. The DNA components of the chimeric genes were "*known* antigen-binding-domain producing DNA and *known* lymphocyte-receptor-protein producing DNA." *Capon* at 1351 (emphasis added). The

Board, however, held that "neither party's specification provides the requisite description of the full scope of the chimeric DNA or encoded proteins...." *Capon* at 1354. In support of their decision, the Board cited *Eli Lilly, Enzo* and other cases as controlling precedent.

In reviewing and overturning the Board's decision, the Federal Circuit held that "[t]he Board erred in refusing to consider the state of scientific knowledge...." *Capon* at 1357. Furthermore, the Federal Circuit stated that the Board's reliance on *Eli Lilly, Enzo* and the other "written description cases" for the case at bar was incorrect and explained that "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e., Regents v. Lilly, Fiers v. Revel, Amgen* [*v. Chugai*], or *Enzo Biochem*, require a re-description of what was already known." *Capon* at 1357. It is particularly noteworthy that the Federal Circuit made this assertion that nucleotide sequences need not be fully presented to satisfy the written description requirement, because the sequences of a sufficient number of sequences of the DNA chimera components were available in the published literature and methods were known and provided for linking the components of the chimera. *Capon* at 1355-1356.

Similarly, the table listed after paragraph 0066 of the published application (U.S. Pre-Grant Publication No. 2004/0191245) lists multiple alleles of HLA (MHC) and their loci. The specification also points the reader to websites that depict the coding sequences of MHC molecules. In addition, methods of generating recombinant proteins were well known in the art at the time of filing. Thus, recombinant MHC molecules themselves were part of "the state of scientific knowledge" at the time of filing the application.

Accordingly, Applicants believe that, in view of properly construed claims and Federal Circuit precedent, the specification fully supports the claimed invention under 35 U.S.C. §112, first paragraph. Applicants respectfully request reconsideration and withdrawal of the written description rejection as it relates to claims 22-47.

B. The Enablement Rejection of Claims 22-47 is Traversed

The Final Office Action of July 6, 2006 rejected claims 22-47 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not "enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims." *Final Office Action of July 6, 2006*, page 4. Specifically, the Office Action states that the specification does not "reasonably provide enablement for all recombinant MHC molecules or functionally equivalent recombinant variants, derivative or fragments thereof or recombinant MHC type molecules or recombinant HLA type molecules." *Final Office Action of July 6, 2006*, page 4.

It should be reiterated that the claims do not recite functionally equivalent derivatives or fragments of MHC molecules. The Office Action's reliance on selected passages from the specification is therefore misplaced and taken out of context, because the cited passage in the Office Action describes "functionally equivalent variants, derivatives or fragments" of MHC molecules, which are not elements of the claim.

Furthermore, the Office Action states that "one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to deplete the anti-MHC antibodies one skilled in the art would have to perform experiments to determine which MHC-type molecules, HLA-type molecules variants, derivatives or fragments did or did not function to bind to the anti-MHC antibodies." *Final Office Action of July 6, 2006*, page 6. The enablement rejection, therefore, appears to be based upon an alleged lack of testing for specific embodiments, rather than "undue experiment." As the Office Action establishes, however, the specification contains several working examples of depleting samples of anti-MHC antibodies using recombinant MHC molecules. Indeed, the application contains at least 4 working examples of recombinant MHC molecules that can be used to deplete anti-MHC antibodies. These working examples of at least 4 recombinant MHC molecules, however, should not limit the scope of the claims solely to constructs comprising these 4 recombinant MHC molecules. Instead, Applicants assert that, given the state of the art at the time of filing, one of skill in the art could use the teachings of the present specification to prepare additional recombinant MHC molecules. The specification is replete with listings of other HLA alleles, *e.g.,* the table listed after paragraph 0066 of the published application (U.S. Pre-Grant Publication No. 2004/0191245), that could be used to generate recombinant MHC molecules. In addition, the

specification directs the reader to various references and web sites that disclose nucleic acid sequences for MHC alleles.

Thus, the specification fully enables the scope of the claimed invention because the specification provides adequate teaching and guidance as to how on one of skill in the art would use a recombinant MHC molecule to deplete a sample of anti-MHC antibodies, which is all that required to enable the full scope of the pending claims. Indeed, the Federal Circuit has stated that "the specification itself [does not] necessarily [need to] describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps …." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

When viewed in the context of proper claim scope and the state of the art at the time of filing, Applicants assert that the application provides ample guidance to one of skill in the art to generate recombinant MHC molecules for their use in the claimed methods of depleting anti-MHC antibodies. Applicants respectfully request reconsideration and withdrawal of the enablement rejection.

C. The Written Description Rejection of Claims 29, 33, 41 and 45 is Moot

The Final Office Action of July 6, 2006 rejected claims 29, 33, 41 and 45 under 35 U.S.C. §112, first paragraph, because the specification allegedly fails to "reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *Final Office Action of July 6, 2006*, page 6-7. Without agreeing with the assertions in the Office Action, Applicants have amended claims 29, 33, 41 and 45 merely to expedite prosecution. The amendments to claims 29, 33, 41 and 45 should not affect applicants right to pursue the broader claims in a related application. In view of the amendments to claims 29, 33, 41 and 45, Applicants assert that the written description rejection is moot. Applicants request reconsideration and withdrawal of the written description rejection as it relates to claims 29, 33, 41 and 45.

D. The Indefiniteness Rejection of Claims 22-47 is Traversed

The Final Office Action of July 6, 2006 rejected claims 22-47 as allegedly indefinite for "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." *Final Office Action of July 6, 2006*, page 8. Specifically, the Final Office Action states that "the recitation 'recombinant MHC-type molecules' is vague and indefinite." *Final Office Action of July 6, 2006*, page 8. In addition, the Final Office Action states that "the recitation 'sufficiently antigenic to be bound' is vague and indefinite. *Final Office Action of July 6, 2006*, page 7. Finally, the Final Office Action states that "the recitation 'recombinant HLA-type molecules' is vague and indefinite." *Final Office Action of July 6, 2006*, page 8.

The three rejections are somewhat related to each other and will be addressed as one argument. Applicants assert that the specification makes clear to one of skill in the art the metes and bounds of the claimed invention. Specifically, the claims and specification state that the antibodies to be depleted are specific for naturally occurring MHC (or HLA) alleles. Indeed, the specification states that "[t]hese recombinant MAC or MHC-type monomers, functioning as anti-MHC antibody antigens, have the advantage that the identity of the MHC is known." United States Pregrant Publication No. 2003/0017447 A1, ¶0017 (emphasis added). Furthermore, the specification indicates that, to detect and deplete anti-MHC (or anti-HLA) antibodies, the recombinant MHC/HLA molecules should maintain "not only residues at the epitopic site, but also key skeletal residues to achieve correct folding of the MHC molecule to form the epitopic site." United States Pregrant Publication No. 2003/0017447 A1, ¶0026. Thus, the specification indicates that, the recombinant MHC molecules should be produced to preserve epitopic sites, *i.e.,* that the recombinant molecules are "sufficiently antigenic." Thus, one of skill in the art would be able to read the claims in light of the specification to determine that the recombinant MHC or HLA molecules used must present a known antigen to the antibodies targeted for depletion. Applicants assert, therefore, that the specification makes clear the metes and bounds of the claims. Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejections.

E. The Obviousness Rejections are Moot

The Final Office Action rejected claims 22-31, 34-43 and 46-47 under 35 U.S.C. §103 as allegedly obvious under a variety cited references. Applicants note that the Office Action establishes that claims 32, 33, 44 and 45 are free of prior art. Applicants have therefore amended independent claims 22 and 36 to recite the limitations of claims 32 and 44 respectively. The amendments to the independent claims, which flow through to the dependent claims, render moot the obviousness rejections in the July 6, 2006 office action. Applicants respectfully request reconsideration and withdrawal of the obviousness rejections.

CONCLUSION

In view of the amendments to the claims, and the arguments presented herein and already or record, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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